

A REVIEW ON MOLECULAR DOCKING ANALYSIS HIGHLIGHTING THE ROLE OF HERBS IN THE CONTROL OF SKIN DISEASES

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Abstract: The chief consideration in formulation technology should be the target site for the product application. Hence molecular docking is the *in silico* method which is highly efficient as compared to the *in vitro* and *in vivo* analysis, it can even discover the active compound in the medicinal plants. The compound is portrayed in three dimensional forms via molecular docking. The usage of computers and software's has led to an increase in computing capabilities that provide opportunities to develop calculations and simulations in the designing of the drug. This method includes a structure based drug design and ligand based drug design¹. To understand the formulation requirements of each body area; several critical concepts must be clarified. First, the anatomy and physiology of the body's various sites must be identified. For instance, is the skin in the area sebaceous gland, transitional between dry and moist, bearing hair, age related, marked by the presence of sweat glands, hormonally mediated, acne prone etc. The second consideration is the dermatological diseases afflicted with the skin area. An ideal skin care product should possess the prescribed medications for the allied diseases condition, but it should also maintain the health of the skin and should also prevent it from the reversibility of the dermatological gridlock. Third, the hygiene of the skin and the mucous present must also be considered very cautiously. Lastly, a through notion should be given on skin health and what requirements it should met to allow it maintain a healthy skin². Only after fulfilling all these conditions a formulation will be issued. Failure to give the necessary consideration will result in a product that meets with initial enthusiasm, due to well-constructed marketing claims, but short-term product performance, may lack efficacy. Although some plants are used in the treatment of various skin diseases, as natural treatment is cheap, safe and efficacious as compared to conventional allopathic drugs. Hence, this review would contain the brief introduction of various parts of the skin and diseases associated with it, herbs used in the treatment for the skin ailments and the *in silico* docking of the same.

Keywords: Herbs, Skin, Molecular Docking, Skin diseases.

INTRODUCTION

Skin is the principal organ of the human body and responsible to act as a barricade against the external environment, while shielding the internal organs as well. Clinical as well as epidemiological studies suggest that the skin exposed to certain reactive oxygen or nitrogen species initiating pollution and stress as well as ultraviolet (UV) radiation provoke harmful effects and lead to intrinsic and extrinsic inflammation, aging, immune-suppression, or even carcinogenesis. In that way, the cosmetic industry is always looking for active ingredients to thwart or decline the hostile outcomes. Also, the demand for cosmetics with natural and organic ingredients is stronger than ever, which now extensively considered as a solemn challenge for the industry³

The facial skin is the thinnest one on the body, except around the eyelids. Thus it could be said that the facial skin is easy to damage but on the other hand also easy to restore its health. The healing process is basic because there is minimum movement of the facial skin. On the other hand, the facial skin is also prone to skin allergies and irritation. So, the facial skin being the thinnest partially allows the penetration of irritants and allergens and makes the formulation development rigid. Skin has basically three layers, the epidermis is the outermost layer of the skin and it provides a waterproof barrier and it crafts the skin tone. Dermis is beneath the epidermis, consisting of sturdy connective tissue, hair follicles and sweat glands. The deeper subcutaneous tissue (hypodermis) is made of fat and connective tissue. The epidermis is mainly derived from surface ectoderm but contains melanocytes of neural crest origin. The dermis is derived from mesoderm and contains collagen, elastic fibers, blood vessels, sensory structures and fibroblasts⁴. Emerging novel strategies are needed to prevent skin diseases represents a desirable goal due to increasing rise in the level of patients throughout the world. The recent trend worldwide has been in favor of phytochemical therapeutics as they are economical and largely free from adverse effects.

BASIC ANATOMY, PHYSIOLOGY AND PROBLEMS:

1. Face

Face is the most complex and challenging area of the body for the researchers and formulators, yet more products are designed for facial use than any other. As the face is the purveyor of our image, our personality, our health, and our age. It identifies who we are, how we are, where we are, and sometimes what we hope to be. From a dermatologic standpoint, the face also possesses some unique medical attributes. It contains all of the glandular structures of the body, including hair, and is characterized by dry skin and transitional skin. The transitional skin is found around the eyes, nose, and mouth. The facial skin is some of the least forgiving when it comes to irritation and allergy. The delicacy of the facial skin that is so desirable for healing purposes allows the ready penetration

of irritants and allergens, making product formulation more challenging. Prominent xerosis lead to what is termed coarse skin while a more even skin surface with smaller pores leads to fine skin and better texture. At the base of the pore lies the hair follicle just below the oily sebaceous gland. The skin lining of the pore connecting the surface to the depth of the follicle is an important transitional area. This is the skin that sloughs improperly creating the environment appropriate for acne. It is also the skin that is easily irritated resulting in the “Breakouts” experienced following the use of products that cause the formation of red bumps, known as papules, and pus bumps, known as pustules⁴

The pore is not only linked to the hair, but also to the sebaceous gland. The sebaceous gland is the structure that produces sebum. Sebum is the oil of the body that lubricates the skin surface, but also provides a food supply for bacteria. The bacteria propionibacterium acnes digest the sebum releasing free fatty acids that initiate inflammation characterized by the influx of white blood cells. These white blood cells form the pus that is seen with acne⁵

The facial skin also contains two types of sweat glands, known as eccrine and apocrine glands. Eccrine glands are the sweat glands that produce a sterile watery liquid associated with the maintenance of body temperature. This apocrine sweat contributes to body odor and allows certain perfumes to smell differently on each individual. The apocrine sweat glands are uniquely located around the eyes.

The skin disease that results from dryness is known as eczema. Eczema is treated by creating an environment suitable for barrier repair to occur. The other common facial skin conditions of acne, acne seborrheic and rosacea, dermatitis are due to a completely different mechanism of action. They may ultimately result in a facial skin barrier defect, but can be considered diseases of the facial skin biofilm. The biofilm is that thin layer of sebum, eccrine sweat, apocrine sweat, skin care products, cosmetics, medications, environmental dirt, bacteria, and fungus that is present on the skin surface. A healthy biofilm will lead to skin health while biofilm abnormalities will eventually lead to disease⁶

2. Eyelids

The eyelid skin is the most interesting part of the body. It moves constantly as the eyes open and close; thus, it possesses unique mechanical properties. It must be thin enough for rapid movement, yet strong enough to protect the tender eye tissues. Eyelid tissue shows the state of health and age of an individual more rapidly than any other skin of the body. Sickly appearance, they are also assessing the appearance of the eyes and the eyelid tissue. The eyelid skin appears to age quickly resulting in the presence of redundant upper eyelid tissue and lower eyelid bags. The redundant upper eyelid tissue is due to loss of facial fat, cumulative collagen loss in the eyelid skin from UV exposure, and the effect of gravity pulling down the upper eyelid skin. Lower eyelid bags are also due to the effect of UV damage and gravity, but edema or swelling may also contribute. This edema may be due to retained body fluids or the release of histamine from inhaled allergens. All of these factors contribute to the complication of the eyelid skin^{7,8}

The eyelid skin also has a paucity of sebaceous glands, making it a common area of skin dryness. The eyelids are also a common source of symptoms induced by allergies. These Symptoms can be itching, stinging, and/or burning. Yet, Eyelids are also a common site for cosmetic adornment. The moisture from tearing wets the eyelid skin and enhances irritant and allergen penetration. The eyes are also uniquely designed to sense substances that might cause vision damage, and thus the eyelids have a heightened immune response.

By far the most common dermatologic disease to afflict the eyelid is eczema, more commonly known as bad dry skin. Since the eyelid is relatively poor in oil glands, drying of the eyelid skin is commonly seen due to over-aggressive removal of lipids. This may be due to the use of a strong or abrasive cleanser or products designed to solubilize oil-based and water-resistant cosmetics, such as mascara and eyeliner. Anything that damages the intercellular lipids or the corneocytes will result in eyelid eczema. Thus, eyelid hygiene must achieve a careful balance between the removal of excess sebum and old cosmetics to prevent eyelash infections and seborrheic blepharitis, while preventing damage to the intercellular lipids and ensuing eyelid eczema.

It should come as no surprise that most men and women notice aging first in the upper and lower eyelid tissue. This thin skin quickly loses elasticity from photodamage, which can be exaggerated by familial tendencies toward eyelid skin laxity, a condition known as blepharochalasis. Eyelid sunscreens must be carefully formulated to avoid allergic and irritant contact dermatitis, stinging, and burning should the product enter the eye, and limited photoprotection. In addition to sunscreens, excellent eyelid skin protection can be obtained by other ways such as through the use of sunglasses and hats.

3. Neck

The neck is an area of highly mobile skin that provides a transition between the thin skin of the neck and the thicker skin of the upper chest and the back. It contains fully mature hairs in the male and thin vellus hairs in the female. It is an important area from a cosmetic standpoint since it is an area affected by shaving in the male, fragrance application in the female, and photo damage in both sexes⁹

The neck skin covers essential underlying structures, such as the blood and nerve supply to the head. The neck also contains the cervical spine and numerous muscles allowing the head to move side to side and up to down. It is also is subject to photo damage, since many forget to wear protective clothing or apply sunscreen to the neck¹⁰

The photo damage state that most commonly affects the neck is known as poikiloderma. Poikiloderma describes the thinned skin present from lost dermal collagen. It resembles chicken skin because the lower dermal oil glands become more visible as little tiny yellow dots. The neck is also the site where men and women apply fragrance. For this reason, the neck is a common site of fragrance allergy. Fragrances can also cause irritant contact dermatitis, which presents as simply dry, red, itchy skin, due to the drying volatile and alcohol based vehicle in the perfume.

The hygiene needs of the neck are similar to the rest of the body. The neck does not contain many oil glands and thus cleansing should be thorough, but not over drying. Probably the most unique hygiene need for the neck area is in males who shave their hair

in that location. The main skin care needs of the neck are good moisturization accompanied by sun protection. The neck receives almost as much sun as the face and is a common site for precancerous and cancerous growths.

4. Lips

The lips present many of the same challenges as lips are instrumental in eating. They contact many different chemicals, foods, and cosmetics. They are also in constant motion, much more so than any other part of the body, due to their participation in the phonation associated with speech. Yet, their cosmetic value cannot be minimized. The lips must sustain pulling, twisting, and contracting forces in many different directions in order to eat and speak. The vermilion is the portion of the lip that is visible and adorned by lip cosmetics. It has a rich vascular supply that is visible through the thin overlying skin. Damage to the lip tissue, from chemicals, sun or cigarette heat, results in formation of a dysfunctional stratum corneum that causes the lip to lose its characteristic red color. This causes a whitening of the lips, medically known as leukoplakia, literally translated as white plaque¹¹

As the lips age, they begin to thin and lose their distinctive shape. This is due to loss of the fat that gives the lip substance. A profile view of a child will reveal lips that protrude from the face, while the profile of a 80-year-old woman will reveal lips that are flat and even depressed from the facial surface. The lip muscles remain intact throughout life, but cannot make up for the loss of the underlying fat suspended over a bony frame. Infection is probably the most common serious lip problem. This is typically due to the herpes simplex type 1 virus that is responsible for fever blisters. This most commonly occurs when the body is sick with another infection, hence the name “fever blister” for the herpes infection. When the body is busy fighting an infection war at another location, the herpes virus takes the opportunity to reproduce and migrate to the lip causing further pain and misery. The fever blister is contagious during the time when the blisters are filled with liquid. This is important to the cosmetic industry, since shared lip balms and lipsticks can transmit the virus as long as the blister fluid remains moist¹²

The lip is also the site of other infections, such as those caused by yeast. Yeast most commonly infects the corners of the mouth, a condition known as perleche. The corners of the mouth are a frequent site of saliva collection. The moisture remains in the mouth corners overnight, creating a condition known as maceration, and provides a perfect environment for the growth of yeast.^{13, 14, 15}

The last common lip disease to be discussed is cheilitis, which simply means inflammation of the lips. Cheilitis can be due to chapped lips, a condition akin to dry skin. This can result from insufficient oil being produced by the tiny yellow oil glands lining the edge of the vermilion border, as seen in elderly individuals, or due to chronic wetting and drying of the lips from lip licking, as seen in children¹⁶

Actinic cheilitis is a precancerous condition that can possibly culminate in skin cancer after years of neglect. Actinic cheilitis are unattractive, since the lips lose their distinct outline and red color, and are best prevented through the use of sunscreen-containing lip balms and opaque lipsticks.

Lips have some unique hygiene needs, because they are the gatekeeper of everything that is consumed orally. Typically, the lips are washed with the face, but they are regularly cleansed with saliva. The best method for keeping the lips infection free is to maintain the vermilion intact, free of fissures or openings.^{17, 18}

5. Scalp

Here the inanimate hair is situated on the animate scalp. The skin necessities of the scalp are complicated due to the presence of abundant sweat, sebum, and nerves all convoluted by the presence of numerous hair follicles. It is beyond the scope of this text to deal with the many issues surrounding hair growth and cleansing, thus this section will focus stringently on the skin forming the scalp. It is imperative to recognize that healthy hair begins with a healthy scalp. The hair grows actually below the skin of the scalp with follicles protected in the subcutaneous fat covering the skull. The scalp has an abundant blood supply to provide the necessary nutrients for hair growth and an extensive nerve network.

These secretions provide nutrients for fungus and bacteria that can infect the skin of the scalp. The hair also increases the chances for infection by providing abundant nourishing surface area for organisms to grow. Lastly, sweat can function as an irritant, accounting for the frequent itching associated with areas of sweat collection, such as the nape of the neck. The presence of the neural network around the hairs also provides more opportunities for sensation of itch to be induced¹⁹

The scalp is the site of many dermatologic diseases, the most common of which is flakes or dandruff. Dandruff lies on a spectrum between occasional mild flaking of the scalp to thick discharge plaques devoid of hair, known as seborrheic dermatitis. These free fatty acids induce irritation, redness, itching, inflammation, and increase the scalp skin turnover resulting in flaking. A mild infection may be perceived as dandruff, but a more severe infection is termed seborrheic dermatitis. The organisms that are the basis for scalp fungal infections can be transmitted person to person via combs or through direct contact. When the scalp is scratched, the skin around the hair is preferentially injured and bacteria from beneath the fingernail placed in the scalp skin causes infection.^{20, 21}

Lastly, no debate of scalp skin could be complete without the mention of psoriasis. As in all other body areas, psoriasis of the scalp is due to the production of poor quality skin very rapidly. It presents with severe thick silvery plaques of scalp scale that may hinder the growth of hair. Cleanliness of the scalp is very important to prevent fungal and bacterial infection that can induce subclinical and clinical disease, without over drying the nonliving hair. It is interesting to note that shaving the hair, which provides a ready surface for infection, can cure many scalp diseases. Certainly, this is not an alternative that would be considered by many!^{22, 23, 24}

The skin care need of the scalp is to exterminate excess skin scale, loosen shedding hair, and maintain the biofilm of sweat, sebum, and organisms in balance. Skin scale provides a good host for the fungal and bacterial organisms and allows sweat and sebum to accumulate on the scalp. Removal of the skin scale is crucial to scalp skin health.^{25, 26}

COMMON INDIAN HERBAL DRUGS FOR SKIN DISEASES

Naturally occurring phytochemicals display an active role in preventive strategy to inhibit, delay, or reverse skin diseases. According to the estimation of the World Health Organization, more than 80% of people in developing countries depend on traditional medicine for their primary health needs.

***Moringa oleifera* (Family- Moringaceae) (Common name- Drum stick tree)**

Moringa is a superfood, it consist of various bioactive compounds such as carotene, vitamin C, vitamin A, tocopherols, phenolics, caortenoids etc . Leaves of Moringa oleifera have potent antioxidants than other parts²⁷ Moringa leaves have been characterized to contain a desirable nutritional balance, containing vitamins, minerals, amino acids, and fatty acids. According to several annotations various preparations of M. oleifera are used for their anti-inflammatory, antihypertensive, diuretic, antimicrobial, antioxidant, anti-diabetic, anti-hyperlipidemic, antineoplastic, antipyretic, anti-ulcer, cardio protectant, and hepato protectant activities. The therapeutic potential of M. oleifera leaves in treating hyperglycemia and dyslipidemia was summarized potential health benefits of M. oleifera, focusing on their nutritional content as well as antioxidant and antimicrobial characteristics²⁸

***Solanum lycopersicum* (Family- Solanaceae) (Common name- Tomato)**

Tomatoes have detoxification effect on the body. Tomato is rich in four major carotenoids alpha- and beta-carotene, lutein, and lycopene, a powerful anti-oxidant which can protect human skin against UVR-induced effects partially mediated by oxidative stress. Tomato is an excellent fruit for rapid skin cell replacement. It acts as natural skin whitening, anti-inflammatory and glowing agent. Tomato juice can be used for healing sunburn because of its unique vitamin C²⁹

***Mangifera indica* (common name-mango) (family-Anacardiaceae)**

Mangiferin has been demonstrated to possess several beneficial properties, including antioxidant, antimicrobial, antidiabetic, anti-allergic, neuroprotective, cardiovascular protective, anticancer, hypocholesterolemic and immunomodulatory effects. The aqueous extract of stem-bark produces a significant anti-inflammatory effect³⁰ Mangiferin exerted protective effects against atopic dermatitis, bronchial asthma, and other allergic diseases. It also protects the body against damage associated with oxidative stress³¹

***Saraca asoca* (Common name- Ashoka) (Family- Caesalpinaceae)**

Saraca asoca has been widely used as traditional Indian medicine especially due to its wound healing properties. Saraca asoca is highly regarded as a universal remedy in the ayurvedic medicine. In the present scenario many plant are used to treat many diseases, but Ashoka is ancient and reliable source of medicine so ashoka is used in many pharmacological activities like eczema, psoriasis, anti-cancer , anti menorrhagic , anti- oxytoxic , anti –microbial activity and have extend uses in ayurveda ,siddha, unani and homeopathy. It have many uses like to treat skin infections, CNS function, genitor-urinary functions .As the global scenario is now changing towards the use of nontoxic and safe plant product having traditional medicine use, development of modern drug from Saraca asoca should be emphasized for the control of various diseases³²

***Curcuma Longa* (Common name- Turmeric, Haldi) (Family- Zingiberaceae)**

Curcumin is an active herbal ingredient possessing surprisingly wide ranges of beneficial properties, including anti-inflammatory, antioxidant, chemo-preventive and chemotherapeutic activity. A growing amount of evidence confirms that curcumin might modulate those phenomena involved in inflammatory, proliferative, and infectious disorders of the skin. Topical application of *C. longa* has been useful in external cancerous skin lesions, psoriasis, and wound healing and plays a very key role in both aging and the main age-related chronic degenerative diseases³³

***Carica papaya* (Common name- Papaya) (Family- Caricaceae)**

Papain in carica papaya has been found to help open clogged pores and is effective in treating blemish-prone skin. This enzyme from papaya (papain) has anti-inflammatory and antibacterial properties. Carica papaya help counteract oxidative stress via various mechanisms of action closely related to its antioxidant properties and eventually improving the management of various oxidative stress-related health conditions. It is also a potential candidate to be exploited for its anti-skin aging specialty, owing to its antioxidant and anti-inflammatory activities³⁴

***Allium cepa* (Common name- Onion) (Family- Liliacea)**

Plant extracts of onion have reputed values for their antifungal, antiprotozoal, antihelminthic, antiviral, disinfectant, and antitumor properties as well as in the treatment of gastric and hepatic disorders, diabetes melitus, hypertension,hypercholesterolemia and immunodeficiency syndromes³⁵

***Beta vulgaris* (Common name- Beetroot) (Family- Chenopodiaceae)**

Beetroot has its potential utility as a health promoting and disease preventing functional food. Beetroot supplementation might serve as a useful strategy to strengthen endogenous antioxidant defenses, helping to protect cellular components from oxidative damage. Beetroot extracts have emerged as potent anti-inflammatory agents. Beetroot is a rich source of phytochemical compounds that includes ascorbic acid, carotenoids, phenolic acids and flavonoids³⁶

***Daucus carota* (Common name- Carrot) (Family- Apiaceae)**

Carrot is a root vegetable with heaps of carotenoids, flavonoids, polyacetylenes, vitamins, and minerals, all of which possess copious amount of nutritional and health benefits. Besides lending truth since the old age that carrots are good for eyes, carotenoids, polyphenols and vitamins present in carrot act as antioxidants, anti-carcinogens, and immunity enhancers. It also has Anti-diabetic, cholesterol and cardiovascular disease lowering, anti-hypertensive, hepato-protective, reno-protective, and wound healing. The anti-bacterial, anti-fungal, anti-inflammatory, and analgesic effects of carrot extracts are also noteworthy³⁷

***Emblica officinalis* (Common name- Indian Gooseberry, Amla) (Family- Euphorbiaceae)**

Amla is the richest source of Vitamin C and it is the powerhouse of antioxidants. There are great number health benefits of phytochemicals extracted from various parts of the plant, especially the fruits, which contain phenolics, flavonoids, tannins, and vitamins that strongly associated with the antioxidant activities, anti-inflammation, anti-diabetes, anticancer, and neuroprotective properties³⁸. Amla is also reported to possess chemopreventive, radio, chemo and immune-modulatory, free radical scavenging, antioxidant, and has anti-mutagenic activities³⁹

***Linum usitatissimum* (Common name- Flaxseed, Linseed, Alsi) (Family-Linaceae)**

Numerous studies on natural products has been performed for wound healing because of the bioactive phytochemical constituents such as alkaloid, essential oils, flavonoids, tannins, saponins, and phenolic compounds. Its antioxidant and anti-inflammatory properties are believed to aid in wound healing. Flaxseed contributes to the wound healing process by the presence of omega 3 fatty acids and flaxseed carbohydrates⁴⁰. Linseed has a marked effect such as antifungal, antitumor, antihypertensive and antidiabetic⁴¹

MOLECULAR DOCKING ANALYSIS

Molecular docking is a valuable tool in present drug discovery. Molecular docking methodologies can be used to detect the interaction between a small ligand and a target molecule and to determine whether they could behave in combination as the binding site of two or more constituent molecules with a given structure. The comparison of docking molecules for proteins, other drug-like molecules, or even fragments from the original molecule enables a pool of prominent candidates to be calculated with listed values. Ligand-protein interactions are involved in many biological processes with consequent pharmaceutical implications. Thus, the scientific community has been putting a great effort into the research of the binding phenomenon during the years, leading to the proposal of several theories characterized by an increasing emphasis on the degree of flexibility of the ligand and protein counterparts. Interestingly, a wide spectrum of molecular binding interactions can be explored with this technique, including lipid-protein, lipid-lipid, enzyme-substrate, drug-enzyme, drug-nucleic acid, protein-nucleic acid, nucleic acid-nucleic acid, protein-drug, and protein-protein potential affinities, with key functions in every molecular biological or biochemical stage, as well as structural coupling^{42,43}

CONCLUSION

This review has offered an outline of various cutaneous formulation issues that must be fought fit thought-out when developing effective products for a given body area. Each major body area has been covered in terms of anatomy and physiology of the anatomic site, common dermatologic disease considerations, and skin care needs. Herbals have great potential to cure different kinds of skin diseases. Some wild plants and their parts are frequently used to treat these diseases. The use of plants is as old as the mankind as natural treatment is cheap, safe and claimed to be efficacious. The docking process involves the prediction of ligand conformation and orientation within a targeted binding site. Hence there remains a significant challenge in the application of these approaches in particular in relation to modern drug discovery.

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